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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,685	05/08/2002	Audrey Goddard	P3230R1C001-168	7534

30313 7590 06/28/2005

KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
IRVINE, CA 92614

EXAMINER	
SEHARASEYON, JEGATHEESAN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,685	GODDARD ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,11-14 and 16-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,11-14 and 16-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/15/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/15/2005 has been entered. An action on the RCE follows.

2. Claims 1-3, 7-10 and 15 are cancelled. Claims 4, 5, 6 and 14 have been amended. Claims 21-31 have been added. Therefore, claims are 4-6, 11-14 and 16-31 are pending.

3. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

5. Applicants request for correction of inventorship under 37 CFR 1.48(b) is acknowledged.

6. The Office acknowledges the submission of the IDS dated 4/15/2005.

Priority

7. Based on the differential mRNA expression in the normal and tumor tissues disclosed in the PCT/US00/23328 filed August 24, 2000, Applicants are entitled to the priority date of August 24, 2000 for nucleic acids only based on the enabling disclosure.

35 U.S.C. § 101 Lack of Utility, withdrawn

8. Claims 4-7, 11-14 and 16-20 are rejected under 35 U.S.C. 101, as lacking utility, withdrawn. Specifically, Applicants assertion that the differentially expressed message

can be used as diagnostic tool for lung and kidney tumors is found to be persuasive.

35 U.S.C. § 112, first paragraph, Enablement withdrawn

9. The rejection of claims 4-7, 11-14 and 16-20 under 35 U.S.C. § 112, first paragraph, for lacking support for either a specific and substantial asserted utility or a well established utility is withdrawn for reasons indicated above in paragraph 8.

35 USC § 112, first paragraph – Enablement, maintained

10. The rejection of claims 4, 5, 7, 14 and 16-31 under 35 U.S.C. 112, first paragraph, because the specification does not enable one of skilled in the art to which it pertains, or with which it is most closely connected, to make and/or use the invention commensurate in scope with these claims. The reasons for this rejection under 35 U.S.C. § 112, first paragraph, are set forth at pp. 16-18 of the previous Office Action (19 January 2005). Specifically, SEQ ID NO: 29 fragments, polynucleotides that are 95 or 99% identical to such or to the full-length cDNA deposited as ATCC 203174, nor polynucleotides which hybridize to any of the above or complement thereof because there is no structural or functional information provided in the specification. In addition, the lack of direction/guidance presented in the specification regarding which variants of polynucleotides of SEQ ID NO: 29 encoded proteins would retain the desired activity, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity, the absence of working examples directed to variants and the breath of claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Although, Applicants have amended the claims to assert that the nucleic acid is more highly expressed in normal lung or kidney tumor compared to lung tumor or normal kidney tissue, there is no way of knowing which, if any variants would have the same property of higher expression in the specific tissue. There is no nexus between the degree of homology and regulation of gene expression. Until one identifies a particular variant that demonstrates a higher expression or not, one of skilled in the art would not know the expression profile of the variant. Modifications to polynucleotides encoding the protein, e.g., by substitutions or deletions, would often result in deleterious effects to overall activity and effectiveness of the protein. Furthermore, it is also well known in the art that hybridization under moderately stringent conditions would yield nucleic acid molecules that are structurally unrelated.

Accordingly, the disclosure fails to enable such a myriad of the claimed nucleic acid molecules that not only vary substantially in length but also in nucleic acid composition and to provide any guidance to one skilled in the art on how to make and use the claimed genus of nucleic acid molecule. Thus, it would require undue experimentation for one skilled in the art to make and use the claimed genus of the molecules embraced by the instant claims. Therefore, the rejections of record are maintained.

35 USC § 112, first paragraph – Written Description, maintained

11. Claims 4, 5, 14 and 16-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the

application was filed, had possession of the claimed invention is maintained. The reasons for this rejection under 35 U.S.C. § 112, first paragraph, are set forth at pp. 18-19 of the previous Office Action (19 January 2005). Briefly, the Applicants were not in possession of all or a significant number of polynucleotides that have 95-99% homology to SEQ ID NO: 29 or the full-length cDNA deposited as ATCC 203174 or fragments of SEQ ID NO: 29 or those polynucleotide which hybridize SEQ ID NO: 29 or to the full length cDNA or deposited as ATCC 203174 or complements thereof and still retain the function of SEQ ID NO: 29.

Applicants discuss the legal standards applied when evaluating Written Description, including the requirement that written description depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure (pages 24, 15 April 2005). The examiner takes no issue with the discussion of general requirements for evaluating Written Description in this case. However, Applicants have not described or shown possession of all polynucleotides 95-99% homologous to SEQ ID NO: 29 or the full-length cDNA or fragments of SEQ ID NO: 29 or those polynucleotide which hybridize SEQ ID NO: 29 or to the full length cDNA deposited as ATCC 203174 and still retain the function of SEQ ID NO: 29. Nor have Applicants described a representative number of species that have 95-99% homology to SEQ ID NO: 29 or those capable of hybridizing to SEQ ID NO: 29 or to the full length cDNA deposited as ATCC 203174 or complements thereof, such that it is clear that they were in possession of a genus of polynucleotides functionally similar to SEQ ID NO: 29.

As discussed in the previous Office Action (19 January 2005) even a very skilled artisan could not envision the detailed chemical structure of all or a significant number of encompassed polynucleotides, and therefore, would not know how to make or use them. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making. The claimed product itself is required. Recitation of the phrase "wherein the isolated nucleic acid is more highly expressed in normal lung or kidney tumor compared to lung tumor or normal kidney tissue," (amended claims, 15 April 2005), is not adequate to describe polynucleotides of the instant invention that have 95-99% homology to the SEQ ID NO: 29 or the full-length cDNA or fragments of SEQ ID NO: 29 or those capable of hybridizing to SEQ ID NO: 29 or to the full length cDNA deposited as ATCC 203174 or complements thereof, since there was no reduction to practice to support the amended claims. Specifically, there is no way of knowing which, if any variants would have the same property of higher expression in the specific tissues. There is no nexus between the degree of homology and regulation of gene expression. Until one identifies a particular variant that is highly expressed or not, one of skilled in the art would not know the expression profile of the variant. The mere sequence alone will not allow one of skilled in the art to predict expression. Applicants made no variant polypeptides, and as recited in the current Written Description Guidelines, Applicants must have invented the subject matter that is claimed and must be in "possession" of the claimed genus (Federal Register, 2001, Vol. 66, No. 4, pages 1099-1111, esp. page 1104, 3rd column).

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12a. Claims 6, 11-14, 16 and 21-27 are rejected under 35 U.S.C. 102(e) as being anticipated by Hillier et al. (AA099445, Pub 05/1997). Hillier et al. discloses a cDNA similar to the instant invention (Appendix A, enclosed). This meets the limitations of claims 6, 11-14, 16 and 21-27 in that it provides the nucleotide which is similar to SEQ ID NO: 29 and contains the cDNA in the instant invention. In addition, it would hybridize under stringent conditions to SEQ ID NO: 29. Therefore, Hillier et al. (AA099445, Pub 05/1997) anticipate claims 6, 11-14, 16 and 21-27.

> (f) he did not himself invent the subject matter sought to be patented.

12b. Claims 6, 11-14, 16 and 21-27 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Based on Applicants provisional application (60/098749) disclosure, it appears that the instant cDNA is derived from the MercK EST clone AA099445 (Appendix A, enclosed). Applicant states that " In light of the sequence homology between the DNA55714 sequence and the Merck EST clone no. AA099445, the Merck EST clone no. AA099445 was purchased and the cDNA insert was obtained and sequenced. The sequence of this CDNA insert is shown in and is herein designated as DNA56862-1343." Therefore, claims 6, 11-14, 16 and 21-27

rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

Claim Rejections - 35 USC § 103

13a. Claims 17-20 and 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable Hillier et al. (AA099445, Pub 05/1997) in view of Benson et al. (U.S. Patent No: 6,468,758).

The teachings of Hillier et al. (AA099445, Pub 05/1997) have been described above in paragraph 12a. However, the reference does not teach expression of the CDNA.

Sambrook et al. teach method steps for expression of isolated DNA sequences in mammalian cells and *E.coli* (Vol. 3, Chapter 16 and 17). The method of Sambrook et al. involves subcloning the desired DNA into an expression vector and transfecting the expression vector into host cells. Subsequently the expressed product is recovered from the culture. Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to subclone the DNA of Hillier et al. into an expression vector and transfect the vector into a host cell and culture the host cells as taught by Sambrook et al., with the expectation producing the protein of interest. One of ordinary skill in the art would have been motivated to produce the protein of interest with the expectation of success as taught by Sambrook et al. Therefore, the instant claims are *prima facie* obvious over Hillier et al. (AA099445, Pub 05/1997) in view of Sambrook et al. (1989).

13b. Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable Hillier et al. (AA099445, Pub 05/1997) in view of Fischer et al. (U.S. Patent No: 5, 876, 932).

The teachings of Hillier et al. (AA099445, Pub 05/1997) have been described above in paragraph 12a. However, the reference does not teach expression of the differential expression of cDNA.

Fischer et al. disclose the PCR amplification of cDNA from two more samples and running them on gels to display the expression difference between the tissues of interest (column 1, lines 31-49). Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to amplify the PCR amplify the cDNA described Hillier et al normal lung, lung tumor tissue, normal kidney and kidney tumor tissue run it on a gel as taught by Fischer et al. to see the differential expression pattern in the normal and diseased tissue. One of ordinary skill in the art would have been motivated to PCR amplify the cDNA of interest with the expectation of success as taught by Fischer et al. Therefore, the instant claims are *prima facie* obvious over Hillier et al. (AA099445, Pub 05/1997) in view of Fischer et al. (U.S. Patent No: 5, 876, 932).

14. No Claims are allowable

Contact information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 6/05

JANET ANDRES
PRIMARY EXAMINER

½ Appendix A

Applicants Copy

NCBI Nucleotide

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

Search Nucleotide for Go Clear

Limits Preview/Index History Clipboard Details

Display GenBank Send all to file

Range: from begin to end ☐ Reverse complemented strand Features: ☐ SNP

☐ CDD ☑ MGC ☐ HPRD ☐ STS

☐ 1: AA099445. Reports zk85f07.r1 Soares...[gi:1645393] Links

```
LOCUS       AA099445                 431 bp    mRNA    linear   EST 11-MAY-1997
DEFINITION  zk85f07.r1 Soares_pregnant_uterus_NbHPU Homo sapiens cDNA clone
            IMAGE:489637 5' similar to contains element PTR5 repetitive element
            ;, mRNA sequence.
ACCESSION   AA099445
VERSION     AA099445.1  GI:1645393
KEYWORDS    EST.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (bases 1 to 431)
  AUTHORS   Hillier,L., Lennon,G., Becker,M., Bonaldo,M.F., Chiapelli,B.,
            Chissoe,S., Dietrich,N., DuBuque,T., Favello,A., Gish,W., Hawkins
            ,M., Hultman,M., Kucaba,T., Lacy,M., Le,M., Le,N., Mardis,E., Moore
            ,B., Morris,M., Parsons,J., Prange,C., Rifkin,L., Rohlfing,T.,
            Schellenberg,K., Soares,M.B., Tan,F., Thierry-Meg,J., Trevaskis,E.,
            Underwood,K., Wohldmann,P., Waterston,R., Wilson,R. and Marra,M.
  TITLE     Generation and analysis of 280,000 human expressed sequence tags
  JOURNAL   Genome Res. 6 (9), 807-828 (1996)
   PUBMED   8889549
COMMENT     Contact: Wilson RK
            Washington University School of Medicine
            4444 Forest Park Parkway, Box 8501, St. Louis, MO 63108
            Tel: 314 286 1800
            Fax: 314 286 1810
            Email: est@watson.wustl.edu
            This clone is available royalty-free through LLNL ; contact the
            IMAGE Consortium (info@image.llnl.gov) for further information.
            Insert Length: 528   Std Error: 0.00
            Seq primer: -28M13 rev2 from Amersham.
FEATURES             Location/Qualifiers
     source          1..431
                     /organism="Homo sapiens"
                     /mol_type="mRNA"
                     /db_xref="GDB:3804224"
                     /db_xref="taxon:9606"
                     /clone="IMAGE:489637"
                     /sex="female"
                     /dev_stage="adult"
                     /lab_host="DH10B"
                     /clone_lib="Soares_pregnant_uterus_NbHPU"
                     /note="Organ: uterus; Vector: pT7T3-Pac; Site_1: Not I;
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                     Site_2: Eco RI; 1st strand cDNA was primed with a Not I -
                     oligo(dT) primer [5'
                     AACTGGAAGAATTCGCGGCCGCCTTTTTTTTTTTTTTTT 3'],
                     double-stranded cDNA was ligated to Eco RI adaptors
                     (Pharmacia), digested with Not I and cloned into the Not I
                     and Eco RI sites of the modified pT7T3 vector. Library
                     went through one round of normalization.  Library
                     constructed by M. Fatima Bonaldo."
ORIGIN
        1 caatgtttgc tatccacctc ccccaagccc ctttacctat gctgctgcta acgctgctgc
       61 tgctgctgct gctgcttaaa ggctcatgct tggagtgggg actggtcggt gcccagaaag
      121 tctcttctgc cactgacgcc cccatcaggg attgggcctt ctttcccccc tcctttctgt
      181 gtctcctgcc tcatcggcct gccatgacct gcagccaagc ccagccccgt gggaaagggg
      241 agaaagtggg ggatggctaa gaaagctggg agatagggaa cagaagaggg tagtgggtgg
      301 gctaggggggg ctgccttatt taaagtggtt gtttatgatt cttatactaa tttatacaaa
      361 gatattaagg ccctgttcat taagaaattg ttcccttccc ctgtgttcaa tgtttgtaaa
      421 gattgttctg n
//
```